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## Abstract of the Disclosure

Systems and methods for establishing and/or maintaining the prediction capability over time of a multivariate calibration model designed for quantitative optical spectroscopic measurement of attributes or analytes in bodily tissues, bodily fluids or other biological samples, which are particularly useful when the spectral absorbance of the attribute or analyte is small relative to the background. The present invention provides an optically similar reference sample to capture the characteristics of instrument and environmental variation and to reduce the effect of such variation on the measurement capability of the model. The optically similar reference is preferably stable over time and is designed such that its optical properties are sufficiently matched to the sample of interest that instrument and environmental variations are captured in the same manner in both the test sample of interest and the optically similar reference sample. The optically similar reference sample may include one or more physical components which are spectroscopically measured in a manner which closely mimics the spectroscopic measurement of the test sample of interest. Spectral similarity may also be achieved by using alternative components with spectral characteristics similar to the components contained in the test sample of interest.

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